

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of Claims

Claims 5 and 8-12 were pending and under active consideration in the subject application. With this submission, claims 5 and 8 have been amended. No claims have been canceled. Claims 13-15 have been newly added. Hence, upon entry of this paper, claims 5, 8-12, and 13-15 will remain pending and under active consideration.

Claims 5 and 8 have been amended to recite an active step of testing if said mammal "can no longer close an ATP-sensitive K⁺ channel due to stimulation by a sulfonylurea receptor 1-binding compound." Support for these amendments can be found in the specification as originally filed, e.g., at page 5, lines 8-10, Example 1 on page 48-51, Example 2 on page 51-53, page 38, lines 3-15; page 39, lines 3-5; and page 47, lines 1-14. Additionally, one of ordinary skill in the art would know how to test if the use of a sulfonylurea receptor 1-binding compound could no longer close an ATP-sensitive K⁺ channel.

Newly added claim 13 has support throughout the specification. Specifically, support for this claim can be found in the specification as originally filed, e.g., at page 47, lines 20-24. Newly added claims 14 has support throughout the specification. Specifically, support for claim 14 can be found in the specification as originally filed, e.g., at page 18, lines 2-4. Finally, newly added claim 15 has support throughout the specification. Specifically, support for claim 15 can be found in the specification as originally filed, e.g. at page 20, compound (9).

These changes are believed to introduce no new matter, and their entry is respectfully requested. Applicant respectfully requests reconsideration of this application in view of the comments that follow.

II. Rejection Under 35 USC § 112

Claims 5 and 8-12 are rejected under 35 USC § 112 as “being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” (Office Action, page 2) Specifically, the Office states “[c]laims 5 and 8 provide for the use of the dipeptidyl peptidase IV inhibitor, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass.” (Office Action, page 3) Applicant traverses the rejection because each independent claim clearly sets forth a testing step and an administration step.

A. Claim Amendment Renders the Objection Moot

Without acquiescing to the propriety of the rejection, Applicant has added the active positive steps of “testing.” This amendment should render the objection moot. Applicant thus respectfully requests withdrawal of the objection insofar as the amendments to claims 5 and 8 render the subject rejection moot.

B. Administration to a Patient “in need thereof”

Without acquiescing to the propriety of the rejection, Applicant has added the term “in need thereof.” This amendment should also render the objection moot. Applicant thus respectfully requests withdrawal of the objection insofar as the amendments to claims 5 and 8 render the subject rejection moot.

III. Rejection Under 35 USC § 103

The Office rejects claims 5 and 8-12 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ahrén *et al.*, *Eur. J. Pharmacol.* 404:239-245 (2000) (“Ahrén”) in view of Nauck *et al.*, *Diabetes Care* 21:1925-1931 (1998) (“Nauck”). (Office Action, page 3) Applicant respectfully traverses this rejection.

A. Current Law Regarding “in need thereof”

In *Jansen v. Rexall Sundown, Inc.* 342 F.3d 1329, at 1334 (Fed. Cir. 2003) the Federal Circuit stated:

[T]he word "thereof" in the phrase "to a human **in need thereof**" should be construed to refer to the treatment or prevention of [the disease]. Finally, that "need" must be recognized and appreciated, for otherwise the added phrases do not carry the meaning that the circumstances of their addition suggest that they carry. In other words, administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing [the disease] is not practicing the claimed method, because Jansen limited his claims to treatment or prevention of that particular condition **in those who need** such treatment or prevention. Thus, the '083 patent claims are properly interpreted to mean that the combination of folic acid and vitamin B[12] must be administered to a human with a recognized need to treat or prevent [the disease].

Thus, the court held that the claims' recitation of a patient or a human "in need" gives life and meaning to the preamble's statement of purpose. MPEP 2111.02

B. Current Obviousness Standard

The Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a), and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed, and specifically stated:

Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to***

combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 418 (2007) (emphasis added). As discussed below, the cited art cannot render the claimed invention obvious.

C. Ahrén and Nauck Do Not Render the Invention Obvious

The Office admits that “neither prior art reference teaches how the dipeptidyl peptidase IV inhibitor is used.” (Office Action, page 3) However, the Office states that the “[previous] amendments of the claims have not altered the scope of the method of the instant claims.” (Office action, pages 3-4) Specifically the Office states that “given that ‘used’ does not circumscribe a positive process step (as discussed above), and therefore the prior art still reads on the instant claims.” (Office action, page 4)

1. Ahrén and/or Nauck do Not Teach All of the Steps in the Claimed Invention

Applicant has amended the claims to include an active positive step of “testing if said mammal can no longer close an ATP-sensitive K⁺ channel due to stimulation by a sulfonylurea receptor 1-binding compound.” The Office admits that “neither prior art reference teaches how the dipeptidyl peptidase IV inhibitor is used.” (Office Action, page 3) Thus, with this amendment, applicant has altered the scope of the method to include a positive step that teaches how the dipeptidyl peptidase IV inhibitor is to be used. As such, applicant believes that both Ahrén 2000 and Nauck cannot render the claimed invention obvious.

Furthermore, Applicant submits that neither Ahrén 2000 nor Nauck disclose or suggest a method of treating diabetes with sulfonylurea secondary failure, or of promoting insulin secretion in a diabetic patient with sulfonylurea secondary failure, by administering a dipeptidyl peptidase IV inhibitor to a mammal or a patient who can no longer close an ATP-sensitive K⁺ channel due to stimulation by a sulfonylurea receptor 1-binding compound.

2. No Motivation to Combine Ahrén with Nauck

The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. KSR. (MPEP 2143.01)

DPP-4 was originally identified as a protein on lymphocytes, and associated with white blood cells in the immune system.¹ In fact, DPP-IV was initially thought to be involved in severe combined immunodeficiency disease. This led some researchers to argue that inhibiting DPP-4 might impair the immune system.² It was only later found on many different types of tissue, including the kidneys, lungs, liver, intestines, pancreas, blood vessels and brain. Additionally, DPP-4 has been shown to have a role in cancer.³

One of skill in the art would not know how to combine the DPP-IV inhibitor of Ahrén with the sulfonylurea secondary failure function of GLP-1 disclosed in Nauck. This is because DPP-IV is found on many different cell types and has several different functions associated with several different disease types.

3. The Claimed Invention Yields Unexpected Results

When one considers the obviousness of a combination of known elements, the operative question is “whether the improvement [in combining elements found in the prior art] is more than the predictable use of [the] elements according to their established functions.” MPEP § 2141(I), citing *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007). “While obviousness does not require absolute predictability, *at least some degree of predictability is required.*” MPEP § 2143.02(II) (emphasis added). Evidence of unexpected results must be weighed against evidence supporting prima facie obviousness in making a final determination of the obviousness of the claimed invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA178) (See also MPEP 716.02(c))

¹ Kameoka, J. et al. “Direct association of adenosine deaminase with a T-Cell activation antigen, CD26” *Science* 1:466-469 (1993).

² <http://www.diabetesselfmanagement.com/Articles/Diabetes-Research/dpp-4-inhibitors/All/> visited October 15, 2009.

³ Pro, B. and Dang, N.H. “CD26/dipeptidyl peptidase IV and its role in cancer” *Histol. Histopathol.* 19(4): 1345-51 (2004); Havre, P.A. et. al. “The role of CD26/dipeptidyl peptidase IV in cancer” *Front Biosci.* 13:1634-45 (2008).

The Office states “the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would be obvious.” (Office Action, page 4) However, the advantages of the claimed invention would not naturally flow from the suggestions of either Ahrén and/or Nauck.

The use of a DPP-IV inhibitor yields unexpected results. Specifically, the use of DPP-IV for the treatment of diabetes with sulfonylurea secondary failure produces lower side effects as compared to treatment with a GLP-1 analogue. In contrast, GLP-1 analogues cause side effects such as vascular complication, hypoglycemia, and vomiting. (Specification page 4, see also *Amori et al.* JAMA 298: 194-206 (2007) at 203) Additionally, neither Ahrén nor Nauck suggest or disclose a method of treating diabetes with sulfonylurea secondary failure, or of promoting insulin secretion in a diabetic patient with sulfonylurea secondary failure by administering a dipeptidyl peptidase IV inhibitor.

Thus, there would have been no reason for one of skill in the art, in view of Ahrén and Nauck, to arrive at Applicant’s claimed methods of treating diabetes with sulfonylurea secondary failure or of promoting insulin secretion in a diabetic patient with sulfonylurea secondary failure. Accordingly, the methods as presently claimed would not have been obvious in light of Ahrén 2000 and Nauck.

In sum, the prior art cited by the Examiner in the obviousness rejection cannot be evaluated in isolation, but must now be considered in light of the objective evidence presented bearing on obviousness. The evidence presented strongly supports a case of non-obviousness. For at least the reasons presented above, applicant believes that the rejection of claims 5 and 8-12 under 35 U.S.C. § 103 has been overcome. Accordingly, Applicant respectfully requests that the Examiner withdraw this rejection.

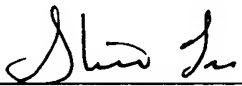
CONCLUSION

Based on the foregoing remarks, Applicant respectfully requests that the Examiner reconsider all rejections and that they be withdrawn. Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

By 

Date October 21, 2009

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

Shine Tu
Registration No. 62,863